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ATTORNEY DOCKET NO.: MBP-1-CIP

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8/14/02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Haas et al

) Examiner: Frank Wei Min Lu

S/N: 09/899,304

) Art Unit: 1634

RECEIVED

Filed: 07/05/2001

) Conf. No.: 3525

AUG 06 2002

Title: "Method for the Targeted Application of
Reagents Onto Immobilized Biological
Material"

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RESPONSE TO RESTRICTION REQUIREMENT
AND
PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, DC 20231

Dear Sir:

In response to the Restriction Requirement dated June 16, 2002, please amend the claims as follows.

IN THE CLAIMS

Please amend claims 1, 3, 4, 8, 10-12, 16-21, 25-29, and 31. Please cancel claims 36-38. For the convenience of both the Examiner and the Applicant, a clean copy of all claims begins on page 2. A marked up copy of the amended claims is also attached.

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1. (Amended) A method for the targeted application of at least one reagent onto immobilized biological material comprising the steps of
 - (a) localizing immobilized biological material selected from the group consisting of cells, cell parts, and chromosomes onto a support slide;
 - (b) placing the support slide having the immobilized biological material onto an optical scanning device;
 - (c) recording electronically the position of an object of interest of the immobilized biological material with respect to the optical scanning device;
 - (d) automatically positioning a micropipette over the position of the object of interest recorded in step (c) and
 - (e) applying the reagent onto the object of interest.
2. The method according to claim 1 wherein the optical scanning device is a microscope.
3. (Amended) The method according to claim 2 wherein a lens position on a turret of the microscope is occupied with a micropipette.
- AZ 4. (Amended) The method according to claim 1 wherein the applying step further comprises applying the reagent in a localized area substantially limited to the position of the object of interest.
5. The method according to claim 1 wherein the step of applying the reagent further includes the use of an automated pipette for dispensing a pre-selected volume of the reagent.
6. The method according to claim 4 wherein the step of applying the reagent onto a localized area further includes placing a cover slip over the immobilized biological material following the step of applying a reagent.
7. The method according to claim 1 further comprising the additional step of photographing the immobilized biological material.
- A3 8. (Amended) The method according to claim 7 wherein the photographs are displayed, thereby providing an additional selection step for selecting only positions corresponding to a selected displayed photograph for the applying step.
9. The method according to claim 1 comprising the additional step of washing the immobilized biological material following an incubation interval.

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10. (Amended) The method according to claim 1 comprising the additional step of washing the reagent applied to the object of interest following application of the reagent.
11. (Amended) The method according to claim 10 comprising the additional step of positioning an analyzing device over the recorded position of the object of interest.
12. (Amended) The method according to claim 1 wherein the object of interest is labeled with a specific marker.

13. The method according to claim 1 wherein the immobilized biological material further comprises metaphase chromosomes.
14. The method according to claim 11 wherein the reagent is selected from a group consisting of a DNA, an RNA, and a polypeptide.
15. The method according to claim 1 wherein the reagent further comprises a plurality of different labelings.

16. (Amended) The method according to claim 15 wherein at least one of said plurality of reagents further comprises a fluorescent dye.
17. (Amended) The method according to claim 14 wherein the reagent specifically binds to the object of interest.

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18. (Amended) The method according to claim 17 wherein the specific binding of the reagent to the object of interest comprises an antigen/antibody reaction.
19. (Amended) The method according to claim 17 wherein the specific binding of the reagent to the object of interest is a hybridization reaction.
20. (Amended) The method according to claim 17 wherein the binding of the reagent to the immobilized object of interest further comprises a ligand/protein reaction.
21. (Amended) A method for the targeted application of at least one reagent onto one or several small regions of interest containing biological objects of interest within a larger region of immobilized biological material comprising the steps of:
 - (a) providing biological material selected from the group consisting of tissue, cells, cell parts, and chromosomes, said biological material immobilized onto a support slide;

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(b) placing the support slide having the immobilized biological material onto an automated optical scanning device;

(c) automatically detecting at least one biological object of interest and recording the position of the at least one biological object of interest with respect to the slide;

(d) automatically positioning a micropipette over the position of said at least one biological object of interest recorded during step (c); and

(e) applying a reagent onto the at least one biological object of interest.

22. The method according to claim 21 wherein the optical scanning device is a microscope comprising a motorized x-y stage and motorized focus control which is connected to a digital image analysis system.

23. The method according to claim 22 wherein a micropipette device is attached to an empty objective position of the objective turret of the microscope and wherein the micropipette is brought into the optical axis of the microscope by switching the objective turret between the observation position and the pipette position.

24. The method according to claim 23 wherein the step of applying the reagent further includes the use of an automated pipette for dispensing a pre-selected volume of the reagent.

25. (Amended) The method according to claim 21 wherein the step of applying the reagent onto said at least one biological object of interest further includes placing a cover slip over the region of interest following the step of applying the reagent.

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26. (Amended) The method according to claim 21 further comprising the additional step of automatically relocating the said at least one biological object of interest to the position recorded in step (c) following said step (e).

27. (Amended) The method according to claim 21 further comprising the additional step of automatically recording an image of the at least one biological object of interest.

28. (Amended) The method according to claim 27 further comprising the additional step of reviewing a gallery of recorded images on a display device for selecting from a plurality of biological objects of interest suited for applying the reagent.

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29. (Amended) The method according to claim 21 wherein the at least one biological material of interest is labeled with a specific marker.
30. The claim according to claim 29 wherein the specific marker is detected by means of a chromogenic or fluorescent dye.
31. (Amended) A method for the targeted application of at least one reagent onto one or several small regions of interest containing biological objects of interest within a large amount of immobilized biological material comprising the steps of:
 - (a) depositing immobilized biological material selected from the group consisting of tissue, cells, cell parts, and chromosomes onto a support slide;
 - (b) placing the support slide having the immobilized biological material onto an automated optical scanning device;
 - (c) automatically detecting [the] biological objects of interest and recording their positions on the slide;
 - (d) automatically marking the positions recorded during step (c) by contacting the slide with a marking device; and,
 - (e) [manually] applying the reagent onto the [regions of interest centered around the] positions that have been marked during step (d).
32. The method according to claim 31 wherein the optical scanning device is a motorized microscope comprising a motorized x-y stage and motorized focus control which is connected to a digital image analysis system.
33. The method according to claim 32 wherein the immobilized biological material is observed under epi-illumination and the marking device is attached to the condenser holder of the microscope and the slide is lowered to bring the marking device into contact with the back surface of the slide.
34. The method according to claim 31 wherein the marking device is a pen.
35. The method according to claim 31 wherein the marking device is a diamond tip.

REMARKS

Applicant has amended claims 1, 3, 4, 8, 10-12, 16-21, 25-29, and 31 which are all drawn to a method for the targeted application of a reagent onto an immobilized biological material. To the extent the Examiner has argued that Groups I and II are a combination and subcombination in view of steps (c) and (d) of claim 1 being performed manually, Applicant has amended claim 1 such that these steps are performed in an automatic manner. Accordingly, Applicant respectfully submits that Groups I and II may be examined together.

In addition, Groups I and III were restricted as being directed to a combination and subcombination. Claim 1 has been amended so that steps (c) and (d) of claim 1 are not performed manually. Accordingly, the grouping of the combination and subcombination no longer have separate utility in that the described steps are done automatically. Accordingly, Applicant respectfully submits that restriction between Groups I and III are no longer required.

With respect to the combination/subcombination restriction requirement of Groups II and III, Applicant disagrees with the Examiner's interpretation that step (e) of claim 31 is performed automatically. Claim 31, as filed, called for manually applying the reagent in step (e). By way of the above amendment, the limitation of manual application in step (e) of claim 31 has been removed. In this regard, claim 31 and claim 21 are identical with respect to a generic step of applying a reagent. In view of this, Applicant fails to see where any combination or subcombination on the basis of step (e) of claims 21 or 31 provide any basis for a restriction requirement.

In summary, Applicant respectfully submits that the original groupings of I, II, and III are, following amendment, suitable for examination together. To the extent Applicant is required to elect one of the groupings initially identified by the Examiner, Applicant elects Group II with the right of traverse. As stated, Applicant believes that following amendments to the claim, the differences between original Groups I through III no longer require a restriction of the claims.

With respect to the species requirement of paragraph 5, Applicant elects the single disclosed species of DNA (claim 14) and affirms that at least claims 1-13 and 15-38 are generic with respect to the elected species.

With respect to paragraph 6 of the restriction requirement, Applicant hereby elects the species of the hybridization reaction (claim 19). Applicant respectfully submits that claims 1-17 and 20-38 are generic and are readable thereon.

Applicant respectfully submits that by way of the above amendment and accompanying remarks, Applicant has responded fully to the Restriction Requirement and election of species requirement. The Examiner is encouraged to contact the undersigned should there be any minor issues which need to be resolved or clarified. Applicant respectfully submits that the application is now in condition for examination with respect to claims 1 through 35.

Respectfully submitted,
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